REDUCTION VENTRICULOPLASTY FOR DILATED CARDIOMYOPATHY: THE BATISTA PROCEDURE

Shahram Salemy

YALE UNIVERSITY

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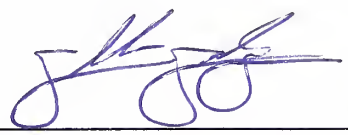

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Shahram Salemy B.S., George Tellides M.D., Ph.D.,
and John A. Elefteriades M.D.

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REDUCTION VENTRICULOPLASTY FOR DILATED CARDIOMYOPATHY: THE BATISTA PROCEDURE. Shahram Salemy, George Tellides, and John A. Elefteriades. Section of Cardiothoracic Surgery, Department of Surgery, Yale School of Medicine, New Haven, CT.

Approximately 50% of individuals with advanced dilated cardiomyopathy die within one year of onset. Reduction ventriculoplasty (Batista procedure) has been proposed as a single discrete intervention that can restore normal cardiac chamber size and function in these patients. We investigated this experimental procedure in patients who were not candidates for the conventional option of cardiac transplantation. Nine patients (8 male, 1 female) with advanced dilated cardiomyopathy underwent reduction ventriculoplasty at our institution from January, 1996 to August, 1997. Mean age was 53 years (range 36-75) and patients were New York Heart Association (NYHA) functional class III (2) or IV (7). Transplantation was not indicated due to patient preference (4), advanced age (2), alcoholism (1), morbid obesity and pulmonary hypertension (1), and bronchopleural fistula with bilateral empyemas (1). Reduction ventriculoplasty was performed by anterior (2) or lateral (7) myocardial resection in conjunction with tricuspid repair (4) or mitral repair (7). Three patients died after 2 days, 11 days and 5 months due to heart failure. Mechanical and pharmacological support was weaned between 0-4 days in 7 patients and one remained dobutamine dependent for 34 days. Patients were discharged home on postoperative day 5-43 (median=13). The 6 surviving patients are in NYHA functional class II (4) and III (2). Serial echocardiography revealed an increase in left ventricular ejection fraction from 15.3% preoperative to 32.5% at 1 year post-reduction ($p< .0005$). Multiple-gated acquisition scanning showed modest decrease in left ventricular end-diastolic volume from 394 ml preoperative to 328.5 ml post-reduction ($p< .3$). Reduction ventriculoplasty improves cardiac size and function with acceptable operative mortality and early survival in high risk patients with non-ischemic dilated cardiomyopathy who are not transplantation candidates.

REDUCTION VENTRICULOPLASTY FOR DILATED CARDIOMYOPATHY: THE BATISTA PROCEDURE

BACKGROUND

In 1999, congestive heart failure continues to be among the most common diseases of man. It is estimated that in the United States alone more than 3 million individuals suffer from congestive heart failure, with more than 400,000 new cases diagnosed per year and an annual mortality rate of 100,000 to 200,000.[1,2] Eighty percent of patients with heart failure are older than 65, and it is the number one discharge diagnosis in that age group. Despite advances in medical treatment, it continues to be a disease of high morbidity and mortality with several studies documenting 24-month mortalities ranging from 10%-50% and 48-month mortalities from 20%-60%.[3-7] Tragically, of those with advanced heart disease (New York Heart Association [NYHA] Class III or IV symptoms) approximately 50% die within one year of onset.[8,9] Finally, it is an expensive health care issue: in 1991, it was estimated that the cost of medical care for patients with heart failure exceeded 5% of the total health care expenditure.[1]

The issue for each clinician is the availability of treatment modalities, both medical and surgical, and which if any of these options can be utilized for an individual patient. A 1995 symposium at the Yale School of Medicine entitled "Advanced Treatment Options for the Failing Left Ventricle" described the current thinking in regards to these treatment modalities.[10] The cornerstone of medical therapy is administration of angiotensin converting enzyme (ACE) inhibitors due to their vasodilator effect and attenuation of

neurohormonal compensatory mechanisms. Beta-receptor blockers also seem to be effective by inhibition of neurohormonal compensatory mechanisms. From a surgical standpoint, if the ventricular dysfunction is related to ischemic, aneurysmal, or valvular heart disease, then coronary artery bypass grafting, left ventricular aneurysmectomy, or valve replacement may be feasible. However, for many cardiomyopathy patients, conventional surgical techniques are not applicable. Heart transplantation yields excellent results but is available for only a fraction of patients with heart failure, and the limited supply of donor hearts has resulted in a large increase of patients on the waiting list, with significant pre-transplant mortality. Mechanical ventricular assist devices and cardiomyoplasty with skeletal muscle flaps are promising experimental approaches, but despite these therapeutic advances, many cardiomyopathy patients are deemed inoperable and rapidly deteriorate on maximum medical therapy.

LAPLACE'S LAW AND THE PHYSIOLOGIC REASONING BEHIND THE BATISTA PROCEDURE

It has long been recognized that the size, shape, and thickness of the left ventricle are important determinants of cardiac function. Early studies applied Laplace's law (tension= pressure x radius) to the heart and concluded that ventricular enlargement resulted in increased wall tension for any given intraventricular pressure. Thus the dilated heart was found to be at a very great mechanical disadvantage compared to the heart with normal dimensions.[11] Suga in 1979 confirmed the importance of ventricular dimensions on cardiac oxygen consumption, and Janz in 1982 validated the importance of ventricular dimensions on myocardial stresses.[12,13] Finally, clinical studies have identified cardiac enlargement as a primary predictor of survival in patients with cardiomyopathies of multiple etiologies.[14-16]

The mechanism of progressive ventricular dilatation has been extensively researched in ischemic cardiomyopathy.[17] Segmental infarction decreases systolic ejection, which increases left ventricular end-diastolic volume and pressure. This leads to increased wall stress, causing both infarct expansion of akinetic segments as well as volume overload hypertrophy of non-infarcted segments. The initial ventricular enlargement or remodeling after myocardial infarction is postulated to represent an adaptive mechanism to increase end-diastolic volume and preserve stroke volume in spite of a decreased ejection fraction.[18] Volume-overload hypertrophy causes ventricular enlargement with an increase in myocardial mass and a lesser increase in wall thickness. This increase in volume with minimal increase in thickness is due to addition of new sarcomeres in series rather than the addition of new myofibrils in parallel, resulting primarily in fiber elongation.[19] The compensatory hypertrophy is insufficient to compensate for the increased ventricular volume and tension, leading to a pathophysiologic sequence of augmented systolic and diastolic wall stresses which stimulate further ventricular enlargement. A positive feedback loop or viscous cycle is created where dilation begets more dilation and promotes ventricular dysfunction.[20] Reversal of this paradigm is clearly beneficial, and while the medical therapies discussed earlier do have some favorable effects, left ventricular aneurysmectomy and reduction ventriculoplasty (the Batista procedure) may be regarded as the surgical solutions for advanced ventricular enlargement which is beyond medical therapy. These operations can, in one discrete intervention, restore left ventricular shape and size, and in many patients improve cardiac function and ultimately clinical outcome.

In order to understand the reasoning and logic surrounding reduction ventriculoplasty, it is essential to review its predecessor: left ventricular aneurysmectomy. Both have been studied by the same group at Yale, and both are based on the same principles described above: essentially, that restoration of proper cardiac chamber shape and size can lead to improvement in the function of that chamber.

LEFT VENTRICULAR ANEURYSMECTOMY

Background

It has been reported that left ventricular aneurysm occurs in 4%-20% of patients following transmural myocardial infarction, although these numbers are decreasing with thrombolytic intervention and early angioplasty.[21,22] The classic complications of left ventricular aneurysm include congestive heart failure, systemic embolization of intracavitary thrombus, angina, and ventricular arrhythmia. Mortality rates are high and variable depending on the study, ranging from 26% to 88% at 5 years depending on the definition of aneurysm, level of ventricular function, and extent of coronary disease.[21-25] Most pertinent to our study is that deaths from congestive heart failure and arrhythmia predominate in all series.

Cooley and colleagues in 1958 were the first to suggest the concept that resection of a left ventricular aneurysm could produce morphological and functional benefits and lead to improved performance of the left ventricle.[26] At that time, Cooley observed that ventricular function was "impaired by the noncontractile sac, which expands paradoxically while the remainder of the ventricle contracts" and that "once the structural abnormality was removed, restoration of the ventricle as a coordinated functional unit was accomplished and ventricular efficiency was improved." There is now a wealth of data from multiple centers that confirms with modern imaging techniques that aneurysmectomy is an important modality in the treatment of the failing left ventricle. Data from Yale University will be discussed as well as similar results from Toronto General Hospital and the Texas Heart Institute.[27-29]

The classical indications for surgical excision of a left ventricular aneurysm have been the major complications: congestive heart failure, embolization, angina, and arrhythmia.[30] Although there has been widespread application in clinical practice and

extensive laboratory investigations, many basic issues regarding left ventricular aneurysmectomy (LVA) remain: (1) Does LVA improve or disturb ventricular morphology and function (does it distort the left ventricular cavity and leave a residual cavity of insufficient volume to permit an adequate stroke volume)? (2) What is the effect of LVA on symptomatic state? (3) What is the effect of LVA on long term survival? These questions are fundamental not only in regards to LVA but also in terms of the evolution of left ventricular reduction surgery from LVA to reduction ventriculoplasty. Analysis of clinical data and application of modern imaging techniques of multi-gated acquisition scanning (MUGA), intraoperative transesophageal echocardiography (ITEE), and magnetic resonance imaging (MRI) have helped to provide new information regarding these issues.

Yale Experience

Seventy-five patients underwent linear LVA at Yale-New Haven Hospital between July 1986 and July 1992.[30] The patients ranged in age from 42 to 84 years (mean 65) and included 54 men and 21 women. Sixty-six aneurysms were anterior (88%) and 9 (12%) were posterior. Indications for surgery (multiple in some patients) included angina in 46 (61%), congestive heart failure in 33 (44%), and ventricular arrhythmia in 41 (55%). Mean preoperative ejection fraction was 24.9% (range 11% to 47%). Associated open heart procedures included coronary artery bypass grafting in 52 patients (69%), directed endocardial resection in 25 (33%), and valve replacement in 4 (5%) (1 aortic and 3 mitral). Ten patients (13%) came to operation with the intra-aortic balloon pump (IABP) in place for therapeutic reasons(angina or pump failure); 39 patients (52%) had the IABP placed prophylactically preoperatively to provide perioperative support.

Hospital mortality was 6.7%, with two deaths due to arrhythmia, one to pump failure, one to atrioventricular groove disruption (associated mitral valve replacement), and

one to fulminant liver failure in a patient with cirrhosis. There were no perioperative cerebral embolic events. Among all patients undergoing LVA, survival (including operative mortality figures) was 86% at one year, 80% at two years, and 64% at five years. Thirty-five of the 37 (95%) surviving patients who had initially presented with angina were improved or angina-free at the time of follow-up. In addition, mean congestive heart failure status (New York Heart association [NYHA] heart failure classification) improved from 3.04 preoperatively to 1.70 postoperatively ($p< 0.0001$).

Data for comparison of preoperative and postoperative left ventricular ejection fraction by MUGA were available in 48 patients. Left ventricular ejection fraction improved from a mean of 24.9% preoperatively to 33.3% postoperatively ($p< 0.0001$). In addition, 28 intraoperative transesophageal echocardiographs (ITEE) were performed, of which 14 were adequate for detailed quantitative analysis. Visual assessment was conducted by an independent cardiac radiologist which revealed that in no case was there distortion of the left ventricular cavity. Visual assessment of global left ventricular contractility revealed immediate improvement in 92% of patients imaged. Eighty-five percent of patients also showed improvement in overall wall segment contractility. Finally, magnetic resonance imaging was conducted on 10 patients and, similar to ITEE, showed normalization of left ventricular size and shape after aneurysmectomy. In no case was distortion from normal anatomic patterns apparent.

The data reported from the Toronto General Hospital and the Texas Heart Institute reported similar findings (Table 1) and so allow us to answer discretely some of the questions posed earlier. First, the hospital mortality from the three institutions was in the range of 5%, a rate consistent with results of prior studies.[31-37] The three series demonstrated that despite advanced left ventricular dysfunction (ejection fraction in the range of 25%) and large proportions of patients with arrhythmia, LVA can be carried out with relative safety.

There was little morbidity directly related to LVA (such as postoperative bleeding, stroke, or infection of the ventricular closure site). Late complications related to aneurysmectomy or its repair were nonexistent. In particular, late stroke did not occur despite policies of not administering anticoagulants postoperatively.

A wide range of mortality rates have been reported for patients who have been treated medically: from 12% to 75% at 5 years.[21-25] Such a wide range of results have hampered comparisons with long term outcomes after LVA. The survival rates in the three series here do compare favorably with general survival expectations for patients who do not undergo surgery and who have severe left ventricular dysfunction, coronary artery disease, arrhythmias, and congestive heart failure. It is however impossible to draw an absolute conclusion without a large controlled clinical trial; such a trial may never be carried out due to the ample data suggesting that prognosis is poor for many patients who are treated medically.

In terms of symptomatic improvement, all 3 series report discrete and significant improvement in exercise capacity. Patients improved at least one full NYHA class, most to NYHA class II or better. Also, most patients became angina free after LVA or after LVA and coronary artery bypass grafting. These improvements in quality of life provide justification for aneurysmectomy independent of survival considerations. Finally all three series reported show a significant, objectively determined improvement in ejection fraction following LVA on the order of one third or more of the preoperative ejection fraction. Such increases are large enough to be clinically relevant and most likely explain the functional improvement in clinical status.

Unifying Hypothesis

There is a large body of evidence to suggest that myocardial infarction with infarct expansion or aneurysm formation leads to a vicious cycle of heart failure.[18,20,38-41] Both infarct expansion and aneurysm formation have severe effects on both the infarct zone and on remote, viable contractile muscle. Laplace's law governs this phenomenon: the increased diameter of the ventricle after aneurysm formation leads to increased wall tension; this increased wall tension depresses the function of the contractile, nonaneurysmal segments of the left ventricle.[42] This process, coupled with the loss of stroke volume consumed in expanding the dyskinetic aneurysmal wall in systole, leads to congestive heart failure. The congestive heart failure leads to fluid retention and further left ventricular dilation, and the viscous cycle continues.

Extension of Indications for Aneurysmectomy

Given this understanding as well as the findings of their LVAs, the Yale authors conclude that LVA constitutes an important therapeutic tool that can, in one discrete intervention, bring left ventricular diameter back toward normal, lower wall tension and hence interrupt the lethal vicious cycle. Secondly, they contend that mere presence of an aneurysm in a patient undergoing revascularization merits LVA (even without the classic indications of congestive heart failure, emboli, angina, or arrhythmia) provided that the aneurysm is discrete and at least moderate in size and that ventricular function outside the infarct zone is reasonably preserved (the finding of high filling pressures in the catheterization laboratory, even in the absence of overt clinical heart failure, provides further support to resect the aneurysm). Finally, the authors believe that LVA may be indicated despite the absence of the classic symptoms previously mentioned in patients not

undergoing surgery for other reasons. They believe that patients with aneurysms should be serially followed by echocardiography and nuclear imaging and the undergo elective LVA to prevent decompensation should there be progressive left ventricular enlargement or decreased ejection fraction. In short, the authors contend that the documented beneficial effects of LVA justify such broader indications for utilization.

Relevance to Reduction Ventriculoplasty

While these data are significant in and of themselves, their relevance extends into the realm of reduction ventriculoplasty. Specifically, (1) the pathophysiologic mechanisms of left ventricular dilatation that are based on Laplace's law, (2) the fundamental of a vicious cycle of left ventricular dilatation and heart failure, and (3) the notion that this cycle can be interrupted in one discrete intervention, with acceptable immediate and long-term mobidity and mortality, in patients who otherwise have a dismal prognosis. The next section will outline the protocol and results of our clinical trial studying the utility and efficacy of reduction ventriculoplasty for dilated cardiomyopathy.

Clinical Protocol For Reduction Ventriculoplasty

Hypothesis

The hypothesis to be tested is that reduction ventriculoplasty is a relatively safe operation and will result in a significant improvement in cardiac structure (left ventricular end-systolic and end-diastolic dimensions) and function (ejection fraction), functional

status (New York Heart Association [NYHA] class I-IV) and quality of life (QOL questionnaire) in patients with advanced dilated cardiomyopathy as compared to the patients' preoperative status on maximum medical therapy. Survival was also compared to historical control patients on maximum medical therapy. The essential principle of the reduction ventriculoplasty operation is that restoration of a normal left ventricular volume to mass ratio will improve the function of the remaining myocardium in patients with advanced dilated cardiomyopathy in the absence of a discrete aneurysm.

Student's Role

The role of the student in this study was a clear and distinct one. Unlike a chart review, the student was involved from the onset of the project in a prospective fashion. He was instrumental in structuring the planning of the investigation including the creation of patient inclusion and exclusion guidelines, questionairres, and follow-up. In addition, he studied both the operative procedure and attended operations and was responsible for the entire data analysis which he provided to the advisor as new data points became available. Also, it is worth noting that the student completed all of these tasks over the course of three years in which there were no published data on the topic. Finally, the student was responsible for helping publish results of the first experience with the Batista procedure in New England.[43]

Protocol

Nine patients with advanced heart failure from dilated cardiomyopathy who agreed to participate in this study and from whom informed consent was obtained had specific evaluations and investigations and underwent reduction ventriculoplasty in addition to any

necessary conventional cardiac surgery. Clinical assessment and investigations of patients continued for up to 24 months.

Reduction ventriculoplasty was performed according to the method of Dr. Randas Batista.[44] The technique, in brief, was as follows. A median sternotomy was made and the pericardium opened. The patients were systemically heparinized and cannulated for bypass. Normothermic cardiopulmonary bypass was instituted and the heart kept beating by immediate defibrillation as required and use of potassium injection into the aortic root. The heart was continuously perfused and no aortic cross-clamping or cardioplegia was utilized. The lateral ventricular wall was sharply incised near the apex of the heart between obtuse marginal artery branches. The incision was continued towards the base of the heart close to the posteromedial papillary muscle under direct vision. The incision was completed by carefully excising the ventricular wall close to the anterolateral papillary muscle and across the base about an inch from the circumflex artery. The wedge-to-oval shaped specimen was removed and further tailoring of the resection margins performed as necessary. Hemostasis of bleeding epicardial artery branches was obtained by cautery. Any thrombus was carefully removed. The ventriculotomy incision was closed with two layers of running prolene sutures without the use of reinforcing felt pledget strips. The patient was weaned off bypass with liberal use of sodium nitroprusside for afterload reduction and isoproterenol for inotropic stimulation. Hemostasis was confirmed and the chest closed in the usual fashion.

Associated conventional cardiac operations were performed as necessary. Tricuspid valvuloplasty was done under total cardiopulmonary bypass prior to reduction ventriculoplasty. Mitral valve repair could be carried out through the ventriculotomy incision as required. Aortic valve repair and replacement or coronary artery bypass grafting could be done conventionally after the reduction ventriculoplasty. Aortic cross-clamping and continuous warm perfusion through a coronary sinus catheter or antegrade and retrograde cold cardioplegia were utilized for these additional procedures.

Patients were evaluated preoperatively and at standard intervals postoperatively. Preoperative evaluation included consultation by the heart failure service and, when necessary, by the electrophysiology service. Clinical assessment and investigations were conducted at intervals as specified in Table 2. This included a history of symptoms, medications and hospitalizations, NYHA functional class, quality of life questionnaire, blood tests as specified, pulmonary function tests, chest roentgenograms, electrocardiograms, right and left heart catheterization, transthoracic echocardiogram, transesophageal echocardiogram, multiple-gated acquisition (MUGA) scanning, chest MRI, exercise test and 6 minute walk. The patients were analyzed and the data evaluated using statistical tools, such as the paired t test, in order to assess the significance of the differences in variables before and after reduction ventriculoplasty.

Subject Population

Of significance is that patients who were not candidates for cardiac transplantation (in particular the elderly or patients with systemic disease processes) were still considered for reduction ventriculoplasty. In addition, concomitant bypass or valve cardiac surgery did not exclude patients from reduction ventriculoplasty.

Patient Inclusion Criteria

- Advanced heart failure due to dilated cardiomyopathy on maximal medical therapy
- NYHA Class III or IV functional status
- AGE > or = 18 years old
- Males or nonpregnant females

- Left ventricular end-diastolic dimension > 5.5 cm
- Left ventricular ejection fraction < 30%
- Peak oxygen consumption (VO2) > 10 and < 22 ml/kg/minute
- Geographic availability for follow-up

Patient Exclusion Criteria

- Age < 18 years old
- Pregnant females
- Cardiac reasons if there was:
    - cardiogenic shock with systolic pressure < 90 mm Hg
    - dependence on intravenous inotropic agents
    - uncontrolled hypertension with diastolic pressure > 95 mm Hg on medications
    - severe pulmonary artery hypertension with systolic pressure > 60 mm Hg
    - severe persistent arrhythmias despite optimal medical treatment
    - cardiac arrest, myocardial infarction, or angioplasty within 3 months
    - previous cardiac surgery
    - hypertrophic cardiomyopathy
    - participation in concurrent cardiac investigational drug study
- Pulmonary reasons if the forced vital capacity was < 50% of predicted value
- Renal reasons if creatinine clearance was < 30 ml/minute or serum creatinine was > 3.0 mg/dl

- Hepatic reasons if hyperbilirubinemia > 3 mg/dl, active hepatitis or severe cirrhosis
- Nutritional cachexia with serum albumin < 2.5 gm/dl
- Neurological reasons if dense stroke or severe dysfunction
- Unresolved psychiatric disease or drug abuse
- Clinically significant multi-organ dysfunction
- Any non-cardiac disease preventing or limiting survival, exercise ability or rehabilitation
- Patient unable or unwilling to comply with the study requirements or protocol

DATA

Nine patients (8 male, 1 female) underwent reduction ventriculoplasty at our institution from January 1996 to August 1997 (Table 3). All were diagnosed with advanced, idiopathic cardiomyopathy, with NYHA functional class III (2) or IV (7). Mean age was 53 (range 36-75), and had the following contraindications to cardiac transplantation: patient preference (4), advanced age (2), alcoholism (1), morbid obesity and pulmonary hypertension (1), and bronchopleural fistula with bilateral empyemas (1). Three were inotrope dependent, 1 was intra-aortic balloon pump (IABP) dependent, and 3 were Intensive Care Unit dependent.

Preoperatively, the mean left ventricular ejection fraction (EF) by echocardiography (ECHO) was 15.3% (range 9%-23%, standard deviation (SD) ± 5.12) and by multiple-gated acquisition scan (MUGA) was 16.9% (range 7%-31%, SD ± 8.96) (Table 3). Mean left ventricular end-diastolic dimension (LVEDD) by ECHO was 7.46 cm (range 6.3 cm-9.6 cm, SD ± .97) and mean left ventricular end-diastolic volume (LVEDV) by MUGA

was 394 ml (range 320 ml- 470 ml, SD ± 47.14). All but one of the nine patients had preoperative evidence of valvular disease by ECHO.

Partial left ventriculectomy was performed by anterior (2) or lateral (7) myocardial resection in conjunction with tricuspid valve repair (4) and mitral valve repair (7) (Table 4). Three patients died after 2 days, 11 days and 5 months due to heart failure. Mechanical and pharmacological support was weaned between post-operative day 0-4 in 7 patients; one patient remained dobutamine dependent for 34 days. Patients were discharged home on postoperative day 5-43 (mean= 13, SD ± 12.3).

Serial echocardiography showed a decrease in mean left ventricular end-diastolic dimension from 7.46 cm preoperatively (n=9, SD ± .97) to 6.46 cm at 2 weeks post-reduction (n=8, $p< 0.0075$, SD ± .46), 6.90 cm at 3 months post-reduction (n=4, $p< 0.15$, SD ± 1.43), and 6.75 cm at 1 year post-reduction (n=2, $p< 0.30$, SD ± 1.63) (Figure 1, Table 5). Echocardiography also revealed an increase in mean left ventricular ejection fraction from 15.33% preoperatively (n=9, SD ± 5.12) to 26.00% at 2 weeks postoperatively (n=5, $p< 0.025$, SD ± 10.29), 26.25% at 3 months postoperatively (n=4, $p< 0.10$, SD ± 3.78) and 32.5% at 1 year post-reduction (n=2, $p< 0.0005$, SD ± 3.54) (Figure 2).

Serial MUGA scans also reported an increase in mean left ventricular ejection fraction from 16.89% preoperatively (n=9, SD ± 8.96) to 21.86% at 2 weeks post-reduction (n=7, $p< 0.15$, SD ± 8.80), 26.25% at 3 months post-reduction (n=4, $p< 0.10$, SD ± 13.77), and 30.5% at 1 year post-reduction (n=2, $p< 0.005$, SD ± 9.19) (Figure 3). Left ventricular end-diastolic volume decreased from a mean value of 393.88 ml preoperatively (n=8, SD ± 47.14) to 374 ml at 2 weeks post-reduction (n=4, $p< 0.5$, SD ± 160.63), 358.33 ml at 3 months post-reduction (n=3, $p< 0.3$, SD ± 107.34) and 328.5 ml at 1 year post-reduction (n=2, $p< 0.3$, SD ± 118.09) (Figure 4). Most importantly from a quality of life standpoint, the 6 surviving patients are in NYHA class II (4) or III (2) (mean = 2.33, $p< 0.0005$, SD ± .52).

DISCUSSION

This section should be approached in the manner in which the operation was conceived: beginning with a theoretical and mathematical discussion, which eventually leads to a discussion of our data and of that from other centers.

Mathematical Analysis and Critique

Laplace's law is as follows:

$$P = \frac{2 * \sigma * h}{R} \quad \text{(equation 1)} \qquad \text{or} \qquad T = P * R \quad \text{(equation 2)}$$

Where h is the wall thickness, σ is the wall stress, P is the transmural pressure, R is the cavitary radius, and T is tension. Regardless of its form, this law states that the larger the cavity (R) and the higher the pressure of the fluid it contains (P), the more the tension (T) on the wall. For the heart, the greater the tension, the greater the force necessary for ejection, thus the greater the need for muscular compensation. This concept is better understood in terms of the pathology behind dilated cardiomyopathy. As the left ventricular chamber enlarges, peak systolic wall stress increases (by the law of Laplace) which then causes myocardial hypertrophy of sufficient magnitude to normalize the systolic stress.[45] The basic principle of the Batista procedure for dilated cardiomyopathy is not to reduce the mass of the ventricle but to reduce the size of the chamber of the dilated

ventricle, thus to reduce the wall stress of the ventricle and to prevent further myocardial hypertrophy and ultimate heart failure, the "vicious cycle" that was discussed earlier.

The reduction of chamber volume, however, is achieved only at the expense of muscle excision. Despite the increase in myocardial mass secondary to chamber enlargement and increased systolic wall stress, the myocardial stress is always higher in patients with dilated cardiomyopathy.[45-49] According to a principle defined by Grant, Greene, and Bunnell and supported by others the normal mass to chamber volume ratio should be maintained in dilated cardiomyopathy.[45,46,50] Kennedy and associates calculated both mean normal values of left ventricular mass/left ventricular end-systolic and end-diastolic volume ratios (LVM/LVESV and LVM/LVEDV) as well as mean myocardial wall stress in survivors and nonsurvivors with dilated cardiomyopathy using the following equation:[48,51,52]

$$\sigma = 1.335 * P_{lv}(1 + [3V_{lv}/V_m]) \qquad \text{(equation 3)}$$

where P_{lv} is instantaneous or mean left ventricular systolic pressure, V_m is the volume of the myocardium, V_{lv} is LVESV, and σ is calculated systolic stress. The mean myocardial wall stress in survivors and nonsurvivors with dilated cardiomyopathy was 541 and 590 kdynes/cm^2, respectively. The calculated value of mean LVM/LVESV ratio in survivors and nonsurvivors with dilated cardiomyopathy was 1.36 and 1.06, respectively. Similarly, in another report concerning patients with compensated dilated cardiomyopathy, the calculated mean LVM/LVESV ratio (1.8) was higher than that (1.09) in patients with decompensated dilated cardiomyopathy.[47] These findings suggest that the previously stated hypothesis is not valid: ventricular mass does increase but not proportionally with the increase in chamber volume (which explains the dilation of the ventricle) and not to the degree required to normalize the systolic stress (hence eventual cardiac decompensation).

We can now use these mathematic and physiologic principles as evidence for the potential benefits that volume reduction surgery can provide. Chanda et al. illustrates the importance of ventricular mass in reduction of systolic stress using the above formula in the following example.[53] In a normal patient with a P_{lv} of 122 mm Hg, a V_{lv} of 45 ml, and an LVM of 164 gm, the calculated systolic stress σ is 306 kdyne/cm^2.[52] In a patient with decompensated dilated cardiomyopathy with P_{lv}= 105 mm Hg, V_{lv}= 300 ml, and LVM=480 gm, the calculated systolic stress would be 414 kdyne/cm^2. In this patient, to keep the systolic stress 306 kdyne/cm^2, an additional 338 gm (i.e. total LVM of 818 gm) would be necessary. With the reduction of LVESV from 300 to 150 ml and LVM from 480 to 300 gm, the left ventricular systolic stress would be reduced from 414 to 359 kdyne/cm^2, if the P_{lv} were to remain 105 mm Hg. This example helps illustrate that in dilated cardiomyopathy, surgical intervention directed to chamber volume reduction, even at the expense of mass reduction, would decrease the myocardial wall stress.

It must be made clear that a reduction in stress does not uniformly equate with a physiologic benefit. For example, removing half of the ventricle of a normal heart would result in a decrease in wall stress, but would clearly not improve its function. The issue then is precisely how dilated must the ventricle be and how much ventricular mass must be removed in order for there to be a beneficial effect? From a vigorous mathematical point of view, the answer is yet to be provided.

Another example can help illustrate the point.[54] In nature, muscle fibers can only generate a certain maximum amount of force per unit surface area (σ_{max}). In order for a heart to generate a non-zero stroke volume, intraventricular pressure must exceed a minimal systemic systolic pressure (P_{min}). On the basis of equation 1, for a sufficiently dilated ventricle:

$$R > \frac{2 * \sigma_{max} * h}{P_{min}}$$

Therefore, as the ventricle continues to dilate (R increases) stroke volume approaches zero. In this limiting case, resection of ventricular mass, by reducing R while keeping h constant, will increase stroke volume to a non-zero value. It follows that if ventricular function were occurring purely on a geometric basis (due to dilation with normal intrinsic fiber contractility), an appropriate resection, such that R/h were corrected to normal, would mathematically lead to a return to normal function.

In short, there are clearly extreme theoretical cases in which the Batista procedure will lead to an increase in function in absolute terms. There are other extremes at which function will be worsened, but in both cases stress can be reduced. Therefore, mathematical stress reduction alone does not imply any particular acute effect on function and therefore not on clinical improvement. With this understanding of the mathematics involved, it is clear that clinical data is required in order to truly assess the efficacy of volume reduction surgery.

The Yale Data

A few points regarding our findings must be made. Firstly, although nine patients underwent the procedure, it is difficult to accurately assess how many patients refused the operation as well as how many patients were denied the operation because they did not meet protocol criteria. Multiple patients evaluated in our offices fell into both categories, but the exact numbers are unclear.

Secondly, there was no appreciable differences in long-term outcome among patients who had refused transplantation compared to those who were simply not

transplantation candidates. Three of the four Batista patients who refused transplantation were alive at one year post-operation, compared to three of the five Batista patients who had not been transplantion candidates. In addition, of the patients alive at one year, there was no difference in cardiac functional class (see Table 5).

Thirdly, although it would be helpful to estimate the theoretical mortality of these patients without surgery, it is extremely difficult to do so. This is an unfortunate but inherent problem to experimental surgical treatments for congestive heart failure, as most if not all studies cannot be randomized. In addition, with such experimental surgery, the number of patients involved is usually quite low and decreases further as follow-up time increases, thus making accurate clear judgement of benefit less and less objective. It should be made clear however that although the number of patients involved in our study appears small, it is quite respectable compared to other academic centers studying this fledgling operation.

In terms of the significance of our data, a few points come to the forefront. First, it was clear ejection fraction was increased as evaluated by both echocardiography (from 15.33% pre-operative to 32.5% post-operative, see figure 2) and MUGA scan (16.89% pre-operative to 30.5% 1 year post-operative, see figure 3). In addition, MUGA scan also revealed a modest reduction in ventricular chamber size as shown in figure 4. In analyzing such results however, the most siginificant indicator (both statistically and clinically) of the efficacy of this intervention must be the reduction in New York Heart Association functional class, most patients being at class II or III at one year post-reduction. This indicator of the patients' quality of life, beyond any other measured outcome, hints to us that the operation had quite a postive impact in the lives of some patients.

Batista Procedure Experience at Other Centers

The application of volume reduction surgery to idiopathic dilated cardiomyopathy was first introduced by Dr. Randas Batista of Brazil. Although he has reportedly performed the operation on over 200 patients, his follow-up evaluation is lacking. His data along with that of the cardiothoracic surgery department at Buffalo was recently reported.[55] Their combined data involved 120 patients with end-stage cardiomyopathy, most of whom were in New York Heart Association (NYHA) class IV. It should be mentioned that 51 of these patients also underwent a valve repair procedure, and that no patients who were awaiting cardiac transplantation were offered the operation, thus selecting for patients with more advanced disease. They reported a 30-day mortality of 22% and a 2-year survival of 55%, with most of the surviving patients either in NYHA class I (57%) or class II (33%). They did report difficulty in obtaining information concerning the Brazilian patients other than the cause of the disease, procedures performed, and crude operative mortality. In addition, they admited that due to limited follow-up, it was not possible to make conclusions regarding long-term outcome of the Brazilian patients. The experience at Buffalo did however suggest that the procedure had merits for selected patients, such as those with dilated cardiomyopathy of a viral or idiopathic cause with or without valvular involvement.

Dr. James McCarthy at the Cleveland Clinic has also studied reduction ventriculoplasty on 57 consecutive patients, the majority of which (95%) had heart failure secondary to idiopathic dilation.[56] All of the patients were either in NYHA class III or IV, and 95% of the patients were awaiting heart transplantation. Notably, 55 of the patients also underwent mitral valve repair at the time of reduction. They reported at 3 months an increase in left ventricular ejection fraction (14% to 23%), a reduction of left ventricular end-diastolic volume (254 ml to 179 ml) and diameter (8.4 cm to 6.3 cm). Cardiac index,

however, did not change (2.2 l/min per m^2). On follow-up, there were 7 late deaths (including 3 sudden deaths) giving an actuarial survival of 82% at 1 year.

G.D. Angelini and colleagues from Bristol conducted the Batista procedure on 14 patients, 7 of which also had a mitral valve repair operation.[57] This group was different from the Cleveland group in that older patients, non-transplant candidates, and ischemic and valvular patients as well as those with cardiomyopathy were operated upon; this was also the case in the Brazil/Buffalo report. All but 3 of the patients survived the operation and one died 3 months later. The others, however, had a significant increase in cardiac index, from 1.91 to 2.27 L/min. per m^2. The authors concluded that the operation might be indicated not only in patients with cardiomyopathy but also in those with ischemic heart disease and in non-transplant candidates.

Synthesis of Clinical Data

Two points regarding these findings must be addressed. First, when analyzing these results it is important to consider the effect of mitral valve repair on outcome, as the majority of patients in our series as well as those in the Cleveland series and many in the Buffalo/Brazil and Bristol series had mitral valve repair. Bolling and co-authors have demonstrated clinical improvement in patients with end-stage cardiomyopathy after mitral valve repair alone and reported an actuarial 1-year survival of 75%.[58] This leads to the valid question of whether or not the positive results are due to the mitral valve repairs. Interpreting the effect of the repair in our series is difficult, as those patients with the mildest mitral regurgitation (see Tables 3 and 5) were either deceased or lost to follow-up. However, in the Cleveland series 27% of their patients had only 0-2+ mitral regurgitation and yet showed significant clinical improvement. This effect is therefore unlikely to be due

to the mitral repair alone. This leads us to believe that the beneficial effects of reduction ventriculoplasty and mitral repair are complementary.

Second, when analyzing the data from the Cleveland and Bristol experiences, one sees a significant improvement in cardiac index in the Bristol patients but not in the Cleveland ones.[59] This difference is probably due to the heterogeneity of the patients in Bristol, with some having ischemic heart disease and localized ventricular dysfunction, which are known to improve after resection of the area. Also, most of the patients in the Bristol group underwent not only mitral valve repair but also another associated procedure, such as coronary artery bypass, tricuspid valve repair, or aortic valve replacement. Since any of these procedures alone, without surgical ventricular reduction, have been associated with remarkable functional improvement and spontaneous left ventricular reduction, it is not possible to determine whether one of the valve procedures, the coronary revascularization, or the ventricular reduction was the most beneficial and specific intervention.[58,60] This concept holds true for all of the reduction ventriculoplasty series to date.

Conclusions

It is clear that congestive heart failure continues to be among the most prevalent of human afflictions and is responsible for a large portion of our yearly national health care expenditure. It is also clear that many of these patients are on maximum medical therapy and have dismal prognoses without cardiac transplantation, which is an extremely limited resource and for which many of these patients simply are not candidates. With this understanding, a surgical procedure that could in one discreet intervention reduce the volume of a dilated heart and improve function both by objective data and by clinical criteria is an attractive proposition. Our data as well as that from other centers have a common

dilemma: while without question reduction ventriculoplasty provides improved cardiac function and quality of life for certain individuals with very advanced disease, predicting exactly which of these individuals will benefit from the procedure has not been elucidated. Indeed, no center to date has been able to accurately predict which patients will benefit from the operation and which will not. A more careful analysis is needed that examines multiple absolute criteria, in particular to specify which cardiomyopathic etiologies and which levels of dilatation can be expected to gain benefit from reduction surgery.

The current thinking regarding the various surgical interventions for dilated cardiomyopathy stand is as follows. Linear aneurysmectomy is reserved for patients with an isolated ischemic aneurysm. Skeletal muscle flap utilization, while once quite promising, have been terminated by the Food and Drug Administration (FDA) due to lack of a clear cut benefit. Mechanical assist devices have been FDA-approved as a bridge to cardiac transplantation. This latest approval has to a certain extent dimmed the enthusiasm surrounding the role of the Batista procedure as the possible primary intervention to bridge cardiomyopathy patients to eventual transplantation. Therefore, while the best recommendation for transplantation candidates is either a transplant or a mechanical heart serving as a temporary bridge to transplantation, if these patients refuse or have a contraindication to the transplant, the Batista procedure can be utilized. Thus, reduction ventriculoplasty will continue to remain an operation with acceptable mortality reserved for patients with advanced disease and on maximum medical therapy without improvement who either refuse or have a clear contraindication to cardiac transplantation.

TABLE 1: Summary of Aneurysmectomy Results from Yale, Toronto, and the Texas Heart Institute

INSTITUTION	Number of Patients	Mean Age	Mean Pre-op EF	Mean Post-op EF	Hospital Mortality	One-year Survival	Five-year Survival
Yale	75	65	25%	33%	6.70%	86%	64%
Toronto	95	58	23%	30%	3%	88%	80%
Texas Heart Institute	252	/	26%	39%	6.8%*	87%	/

Key:

*: includes only patients less than 70 years old
Pre-op: preoperative
Post-op: postoperative
EF: ejection fraction
/: not applicable

TABLE 2: Clinical Assessment and Investigations

TEST	3 months pre-op	2 weeks post-op	3 months post-op	6 months post-op	12 months post-op	18 months post-op	24 months post-op	36 months post-op	48 months post-op	60 months post-op
Clinical Assessment*	X	X	X	X	X	X	X	X	X	X
Blood Tests**	X	X								
ECG	X	X		X	X		X			X
CXR	X	X								
PFT	X									
QOL	X			X	X		X			X
Max. Exercise	X			X	X		X			X
6 min. Walk	X			X	X		X			X
R & L Cath	X									
MUGA	X	X	X		X		X			X
ECHO	X	X	X		X		X			X
MRI	X	X	X		X		X			X

* Clinical Assessment:

1. Patient Status
2. New York Heart Association Class
3. Medications
4. Medical events and symptoms
5. Hospitalizations

** Blood Tests:

1. Complete blood count, PT/PTT
2. Bleeding Time
3. Electrolyte Panel
4. Arterial Blood Gas
5. Clot to Blood Bank

KEY:

pre-op: preoperative
post-op: postoperative
ECG: electrocardiogram
CXR: chest x-ray
PFT: pulmonary function test
QOL: quality of life survey
Max. Exercise: maximum exercise tolerance
6 min. Walk: 6 minute walk test
R & L Cath: right and left heart catheterization
MUGA: multiple-gated acquistion scan
ECHO: transthoracic echocardiography
MRI: magnetic resonance imaging of chest

TABLE 3: Pre-Reduction Patient Profiles

	JH	PP	DD	ER	AM	ET	NP	PS	JB
Age	54	45	46	36	41	58	75	75	49
Sex	M	F	M	M	M	M	M	M	M
CM Etiology	Idiopathic	Idiopathic	Idiopathic	Idiopathic	Idiopathic	Idiopathic	Idiopathic	Idiopathic	Idiopathic
Years of CHF	4	7	2	2	7	7	17	2	3
Contra TX	Bilateral empyemas	Morbid Obesity Pulm HTN	Patient preference	Alcoholism	Patient preference	Patient preference	Age	Age	Patient preference
PMH/PSgH	MI 5/95 Pacer	HTN, Aflut DVT/PE IVC F	HTN Reiters Syndr	HTN PE/IVC F	HTN/Coarct'81 AVR/Root '89	Nonsustained VT	Afib x 3 mon Sternal Fx	Afib x 3 mon CRF, LGIB	HTN
NYHA Class	IV	IV	III	IV	IV	IV	IV	IV	III
ICU Dep	12/17/95	7/17/96	Pre 8/14/96	8/19/96	No ICU	No ICU	No ICU	No ICU	No ICU
Inotrope Dep	12/17/95	No Inotropes	No Inotropes	8/21/96	No Inotropes	No Inotropes	No Inotropes	7/30/97	No Inotropes
IABP Dep	12/21/96	Pro 7/23/96	Pro 8/14/96	Pro 9/10/96	Pro 12/12/96	Pro 6/15/97	8/13/97	Pro 8/22/97	Pro 9/11/87
...ECHO									
LVEF (%)	10	15	10	9	15	23	21	15	20
LVEDD (cm)	7	7.1	7.7	7.6	9.6	6.8	6.3	8.1	6.9
Valves	normal	3+TR, 3+MR	1+TR, 1+MR	3+TR, 3+MR	1+TR, 1+MR	2+TR, 4+MR	1+TR, 2+MR	1+TR, 3+MR	1+MR
...MUGA									
LVEF (%)	10	17	31	7	9	20	12	15	31
LVEDV(ml)	unavailable	408	320	336	409	470	404	414	390
OR	1/31/96	7/24/96	8/15/96	9/11/96	12/12/96	6/16/97	8/14/97	8/22/97	9/12/97

Key:

CM: cardiomyopathy
CHF: congestive heart failure
Contra TX: contraindications to cardiac transplantation
PMH/PSgH: past medical history/past surgical history
NYHA: New York Heart Association
ICU Dep: Intensive Care Unit Dependent
Inotrope Dep: Inotrope Dependent
IABP Dep: Intra-aortic ballon pump dependent
ECHO: transthoracic echocardiography
LVEF: left ventricular ejection fraction

Key (continued):

LVEDD: left ventricular end-diastolic volume
MUGA: multiple-gated acquistion scan
LVEDV: left ventricular end-diastolic volume
OR: date of operation
Pulm HTN: pulmonary hypertension
MI: myocardial infarction
Aflut: atrial flutter
Coarct'81: aortic coarctation repair in 1981
Afib: atrial fibrillation
DVT: deep venous thrombosis

Key (continued):

PE: pulmonary embolus
IVC F: inferior vena cava filter
AVR/Root'89: aortic valve and root repair in 1989
VT: ventricular tachycardia
Sternal Fx: sternal fracture
CRF: chronic renal failure
LGIB: lower gastrointestinal bleed
Pro: prophylactic
TR: tricuspid regurgitation
MR: mitral regurgitation

TABLE 4: Operative and Immediate Postoperative Data

	JH	PP	DD	ER	AM	ET	NP	PS	JB
Procedure	Ant RVP	Lat RVP	Ant RVP	Lat RVP	Lat RVP	Lat RVP	Lat RVP	Lat RVP	Lat RVP
Addl Procedure	TVR	TVR, MVR	MVR	TVR, MVR	MVR	MVR	LVAD	MVR	MVR, TVR
Bypass Time(min)	73	70	41	66	165	113	90	81	79
Cross Clamp(min)	0	0	0	0	83	81	0	0	0
TEE	10% LVEF	15% LVEF	<15% LVEF	<10% LVEF	10% LVEF	15% LVEF	16% LVEF	10% LVEF	20% LVEF
	2+TR, 1+MR	3+TR,3+MR	1+TR,1+MR	2+TR,2+MR	0TR, 0MR	4+MR	3+MR	1+MR	3+TR, 1+MR
...Post-Op									
Extubation	POD#2	POD#1	POD#0	POD#2	POD#1	POD#1	NO	POD#1	POD#0
IABP Removal	POD#3	POD#0	POD#0	POD#3	POD#1	POD#1	NO	POD#1	POD#0
Inotropes Off	POD#2	POD#1	POD#1	POD#2	POD#4	POD#3	NO	POD#34	POD#1
Addl Procedure	None	ICD 7/29/96	None	ICD 9/25/96	None	ICD 6/20/97	Reexploration	PEG	None
Op Mortality	POD#11	No	No	No	No	No	POD#2	No	No
Hosp. Stay(days)	58	18	6	38	18	12	N/A	65	6
Post-Op Stay(days)	11	9	5	15	9	8	N/A	43	5

Key:

Ant: anterior
Lat: lateral
Addl: additional
RVP: reduction ventriculoplasty
TVR: tricuspid valve repair
MVR: mitral valve repair
LVAD: left ventricular assist device
TEE: transesophageal echocardiography
LVEF: left ventricular ejection fraction
TR: tricuspid regurgitation
MR: mitral regurgitation
POD: postoperative day
IABP: intra-aortic ballon pump
Op: operative
Hosp: hospital
Post-op: postoperative
ICD: cardiac defibrillator
PEG: percutaneous endoscopic gastric feeding tube placement

TABLE 5: Postoperative Follow-Up Data

	JH	PP	DD	ER	AM	ET	NP	PS	JB
LVEDD by ECHO (cm)									
Pre-Op	7	7.1	7.7	7.6	9.6	6.8	6.3	8.1	6.9
2 weeks post-op	7	6.2	6.4	5.8	7.2	6.3	deceased	6.2	6.6
3 months post-op	deceased	5.5	7.1	6.2	8.8	LTFU	deceased	LTFU	LTFU
1 year post-op	deceased	5.6	7.9	LTFU	deceased	LTFU	deceased	LTFU	LTFU
LVEF by ECHO (%)									
Pre-Op	10	15	10	9	15	23	21	15	20
2 weeks post-op	22	30	40	26	12	unavailable	deceased	unavailable	unavailable
3 months post-op	deceased	35	20	40	10	LTFU	deceased	LTFU	LTFU
1 year post-op	deceased	30	35	LTFU	deceased	LTFU	deceased	LTFU	LTFU
LVEF by MUGA (%)									
Pre-Op	10	17	31	7	9	20	12	15	31
2 weeks post-op	unavailable	30	27	15	9	25	deceased	15	32
3 months post-op	deceased	35	20	40	10	LTFU	deceased	LTFU	LTFU
1 year post-op	deceased	37	24	LTFU	deceased	LTFU	deceased	LTFU	LTFU
LVEDV by MUGA (ml)									
Pre-Op	unavailable	408	320	336	409	470	404	414	390
2 weeks post-op	unavailable	293	241	358	604	unavailable	deceased	unavailable	unavailable
3 months post-op	deceased	277	480	318	LTFU	LTFU	deceased	LTFU	LTFU
1 year post-op	deceased	245	412	LTFU	LTFU	LTFU	deceased	LTFU	LTFU
Current Status	deceased	alive	alive	alive	deceased	alive	deceased	alive	alive
NYHA Class	N/A	II	II	II	N/A	III	N/A	III	II

Key:

LVEDD: left ventricular end-diastolic dimension
ECHO: transthoracic echocardiography
pre-op: preoperative
post-op: postoperative
LTFU: lost to follow up
LVEF: left ventricular ejection fraction
MUGA: multiple-gated acquistion scan
LVEDV: left ventricular end-diastolic volume
NYHA: New York Heart Association

FIGURE 1: Left Ventricular End-Diastolic Dimension (LVEDD) by Echocardiography

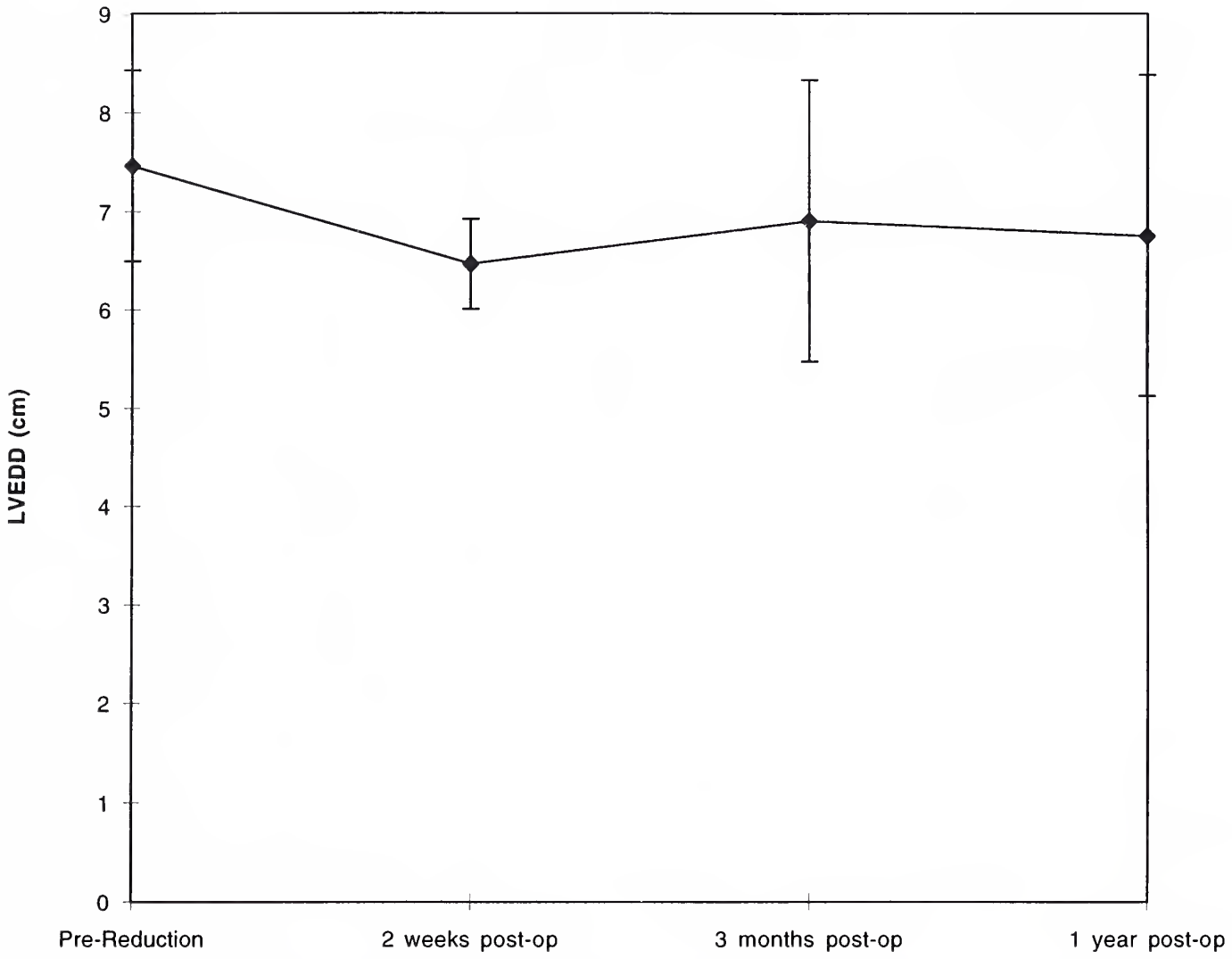


FIGURE 2: Left Ventricular Ejection Fraction (EF) by Echocardiography

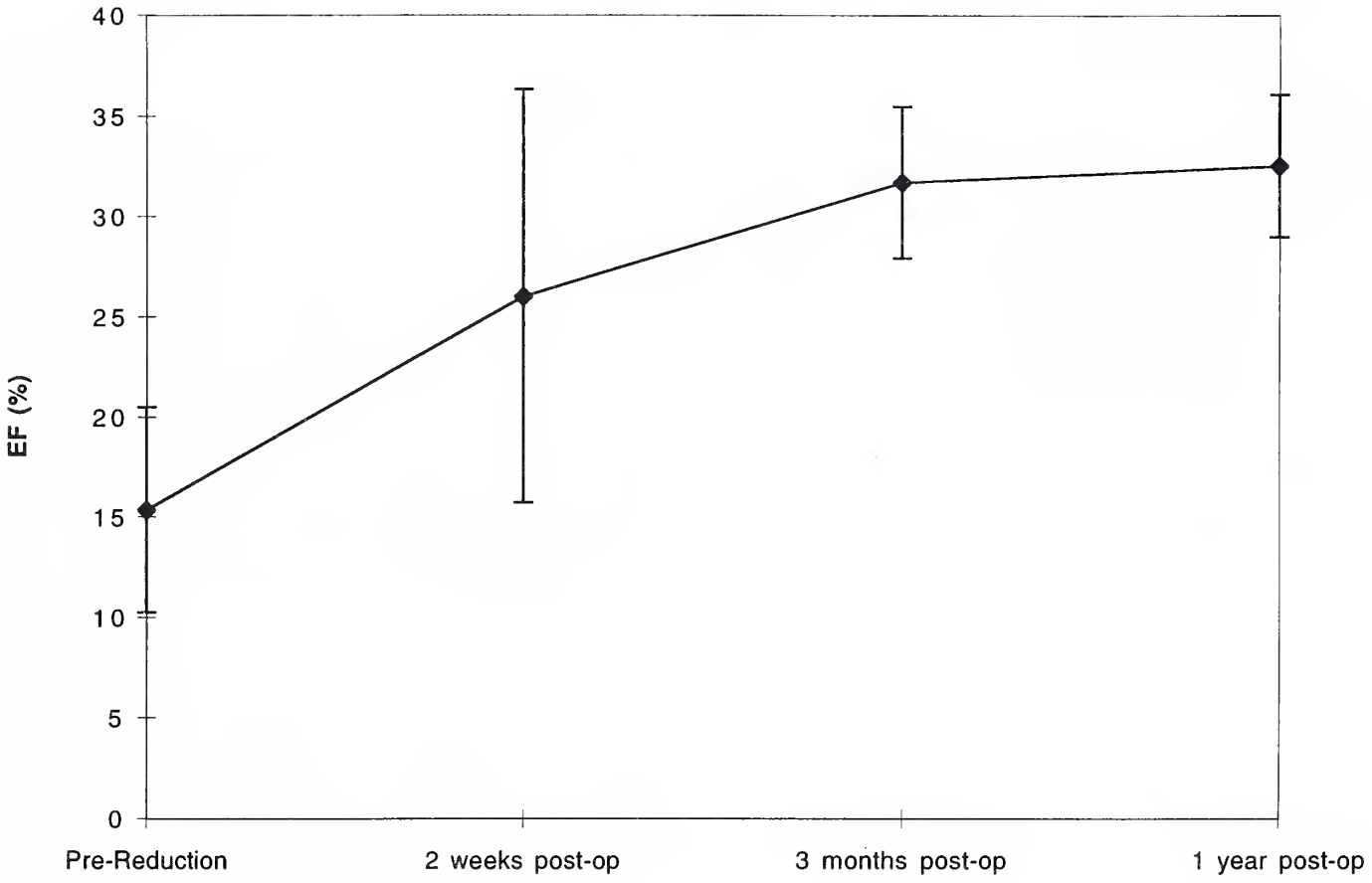


FIGURE 3: Left Ventricular Ejection Fraction (EF) by Multiple-Gated Acquistion (MUGA) Scan

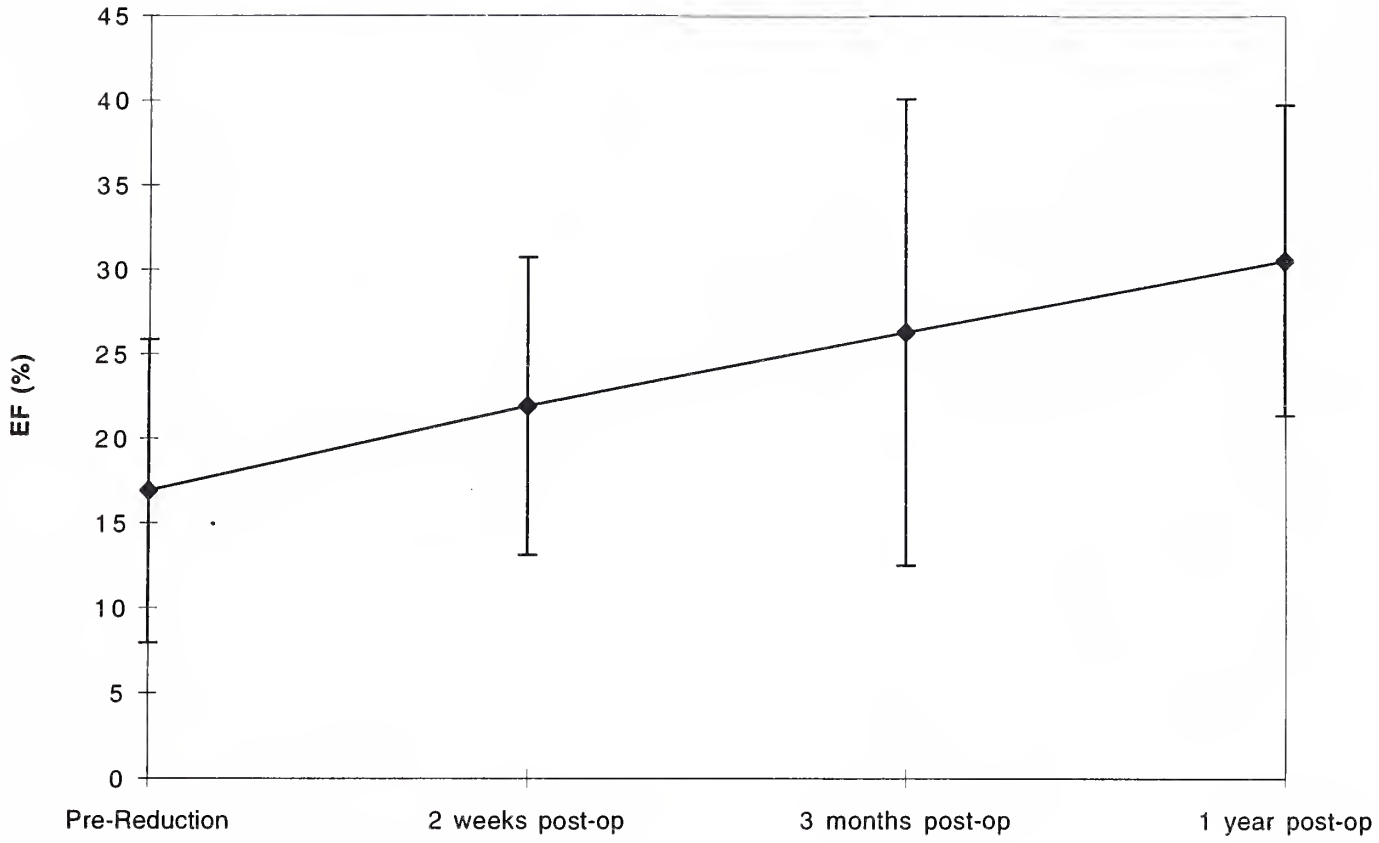
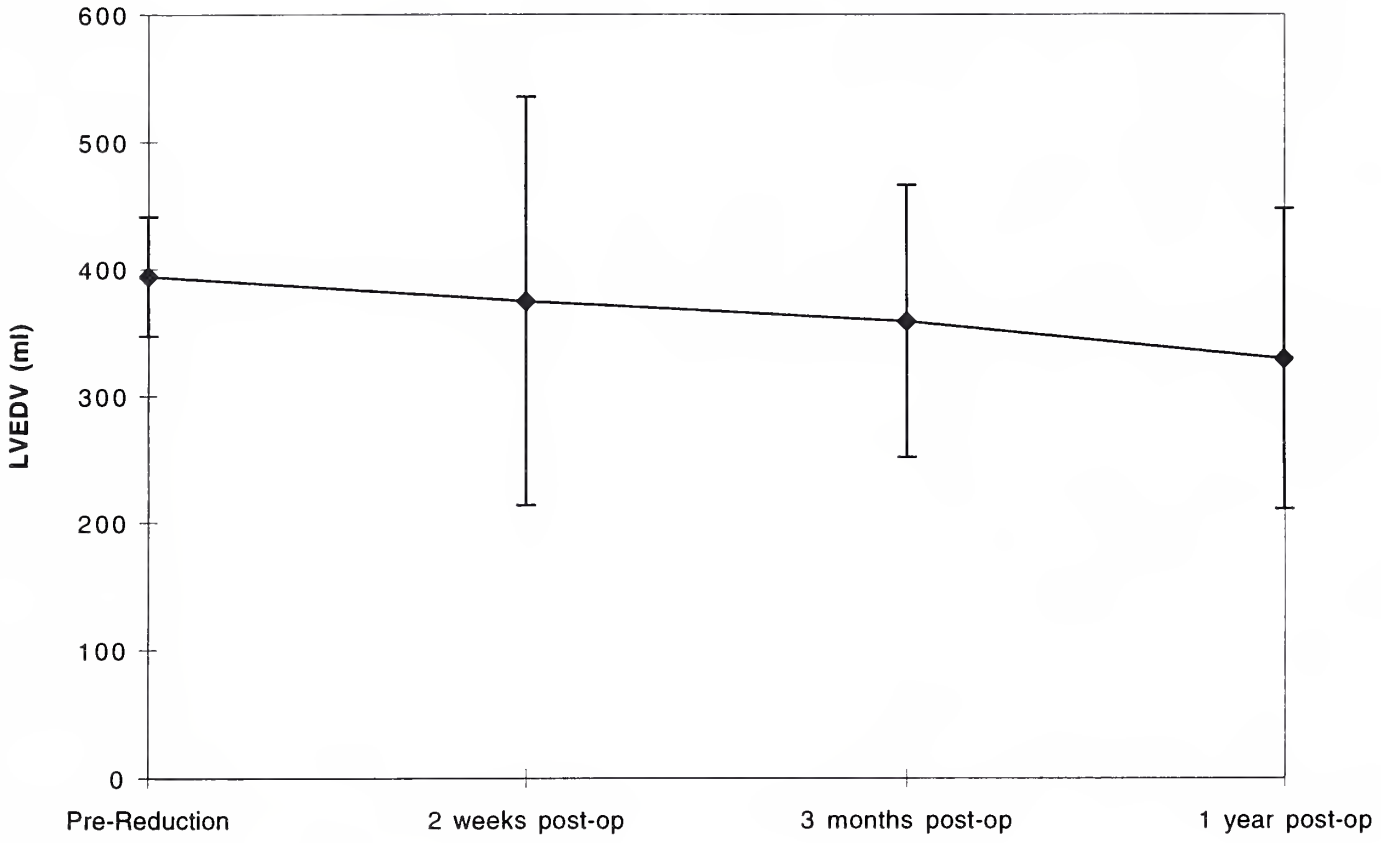


FIGURE 4: Left Ventricular End-Diastolic Volume (LVEDV) by Multiple-Gated Acquistion (MUGA) Scan



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